Humboldt-Universität zu Berlin
U30051PCT

Claims

1. Use of a substance or composition comprising one or more proteasome inhibitors for the manufacture of a medicament for the treatment of an individual infected with a virus selected from the group comprising varicella zoster virus, human cytomegalovirus, HHV6 and 7, Epstein-Barr virus and HHV8.

2. Use of a substance according to claim 1, wherein the individual is a human and the virus is human cytomegalovirus.

3. Use of a substance according to claims one or two, wherein the individual has undergone organ transplantation, is receiving immuno-suppressing chemotherapy, is otherwise immuno-suppressed, has a septic disease or has AIDS.

4. Use of a substance according to any of the preceeding claims, wherein the proteasome inhibitor is selected from a group comprising substances which are able to block the enzymatic activity of the 26S proteasome complex and/or block enzymatic activity of the 20S proteasome core structure.

5. Use of a substance according to any of the preceeding claims, wherein the proteasome inhibitor is selected from a group comprising:

   a) naturally occurring proteasome inhibitors comprising:
   peptide derivatives which have a C-terminal expoxy keton structure, β-lacton-derivatives, aclacinomycin A, lactacystin, clastolactacystein;

   b) synthetic proteasome inhibitors comprising:
   modified peptide aldehydes such as N-carbobenzoxy-L-leucinyl-L-leucinyl-L-leucinal (also referred to as MG132 or zLLL), or the boric acid derivative of MG232, N-carbobenzoxy-Leu-Nva-H (also referred to as MG115), N-acetyl-L-leucinyl-L-leucinyl-L-norleucinal (also referred to as LLnL), N-carbobenzoxy-Ile-Glu(OBut)-Ala-Leu-H (also referred to as PS-1);

   c) peptides comprising:

an α, β,-epoxyketone-structure, vinyl-sulfones such as, carbobenzoxy-L-leucinyl-L-leucinyl-L-leucin-vinyl-sulfon or, 4-hydroxy-5-iodo-3-nitrophenylacetyl-L-leucinyl-L-leucinyl-L-leucin-vinyl-sulfon (NLVS);

d) Glyoxal- or boric acid residues such as: pyrazyl-CONH(CHPhe)CONH(CHisobutyl)$B(OH)_2$ and dipeptidyl-boric-acid derivatives;

e) Pinacol-esters such as: benzyloxycarbonyl(Cbz)-Leu-leuboro-Leu-pinacol-ester.

6. Use of a substance according to claim 4 wherein the proteasome inhibitor is selected from a group comprising:

a) epoxomicin ($C_{28}H_{86}N_4O_7$) and/or

b) eponemycin ($C_{20}H_{36}N_2O_5$).

7. Use of substance according to claim 4, wherein the proteasome inhibitor is selected from a group comprising:

a) PS-314 as a peptidyl-boric-acid derivative which is N-pyrazinecarbonyl-L-phenylalanin-L-leuzin- boric acid ($C_{19}H_{25}BN_4O_4$);

b) PS-519 as a β-lacton- and a lactacystin-derivative which is 1R-[1S, 4R, 5S] -1-(1-Hydroxy-2methylpropyl)-4-propyl-6-oxa-2azabicyclo[3.2.0]heptane-3,7-dione ($C_{12}H_{19}NO_4$);

c) PS-273 (morpholin-CONH-(CH-naphthyl)-CONH-(CH-isobutyl)-$B(OH)_2$) and its enantiomere;

d) PS-293;

e) PS-296 (8-quinolyl-sulfonyl-CONH-(CH-napthyl)-CONH(-CH-isobutyl)-$B(OH)_2$);

f) PS-303 (NH_2(CH-naphthyl)-CONH-(CH-isobutyl)-$B(OH)_2$;

g) PS-321 as (morpholin-CONH-(CH-napthyl)-CONH-(CH-phenylalanin)-$B(OH)_2$);

h) PS-334 (CH_3-NH-(CH-naphthyl-CONH-(CH-Isobutyl)-$B(OH)_2$);

i) PS-325 (2-quinol-CONH-(CH-homo-phenylalanin)-CONH-(CH-isobutyl)- $B(OH)_2$;

j) PS-352 (phenyalanin-CH_2-CH_2-CONH-(CH-isobutyl)l-$B(OH)_2$;

k) PS-383 (pyridyl-CONH-(CH_pF-phenylalanin)-CONH-(CH-isobutyl)-$B(OH)_2$);

l) PS-341; and

m) PS-1 Z-Ile-Glu(O*t*Bu)-Ala-Leu-CHO;
PS-2 [Benzyloxycarbonyl)-Leu-Leu-phenylalaninal or Z-LLF-CHO or Z-Leu-Leu-Phe-CHO PS-1.

8. Use of a substance according to claim 7, wherein the substance is selected from the group comprising:

a) PS-341 and

b) PS-1 Z-Ile-Glu(O*t*Bu)-Ala-Leu-CHO;
PS-2 [Benzyloxycarbonyl)-Leu-Leu-phenylalaninal or Z-LLF-CHO or Z-Leu-Leu-Phe-CHO PS-1.

c) PS-519 as a β-lacton- and a lactacystin-derivative which is 1R-[1S, 4R, 5S]-1-(1-Hydroxy-2methylpropyl)-4-propyl-6-oxa-2azabicyclo[3.2.0]heptane-3,7-dione ($C_{12}H_{19}NO_4$)